Biomagnetic research in gastroenterology

O.Baffa[1] and R. B. Oliveira[2]

[1]*Depto. de Física e Matemática, Faculdade de Filosofia, Ciências e Letras de Ribeirão Preto,* [2]*Depto. de Clínica Médica, Faculdade de Medicina de Ribeirão Preto, 14040-901 Ribeirão Preto-SP, Brazil.*

Thanks to the revolutionary advances in our understanding of Helicobacter pylori, what is really left in the upper GI tract are indeed motility problems. R.W. McCallum, Scand. J. Gastroenterol 30 (suppl 230), v,1995.

1 Introduction

Humans rely on their gastrointestinal system for providing the body with a constant supply of nutrients, water and electrolytes. The food must be digested (reduced physically and chemically to a molecular level) to be absorbed in the small intestine. Since both digestion and absorption depend on diffusion the flow of nutrients along the small intestine (GI transit) must be compatible with the rates of both these processes.

GI transit depends on motions of the intestine walls, caused by contractions and relaxations (motor activity) of the muscle layers, which in turn are governed by electrical signals. So far in the clinical routine, GI transit has been studied by methods based on X-rays and radioisotopes, and motor activity by means of pressure recordings obtained by catheters passed by mouth or nostrils. Moreover, electrical activity recordings present important drawbacks.

The use of magnetic measurements to study the gastrointestinal tract can be divided in two categories, one concerned with magnetic fields produced intrinsically by the electric currents of organs and the other with magnetic fields produced by magnetic materials that are ingested. In the first group, magnetic measurements are used to detect electric currents associated with the gastrointestinal tract. In the second group, the fields produced by ingested magnetic markers (MM) or tracers (MT) can be measured at the surface of the torso, allowing determination of the position, time course, quantity and state of order yielding information about the gastrointestinal motility. Biomagnetic techniques in some cases can represent an alternative, and in others a unique way to study the gastrointestinal tract. It is interesting to note that the scenario provided by GI applications of biomagnetism integrate all the possible fields yet measured in humans: those from electric current as in the brain and heart, those from paramagnetic substances as in the case of the liver and, finally, magnetic fields produced by ferromagnetic particles as in the case of magnetic markers and tracers. There is hope that in the future more information about the GI tract or even more comfortable exams would be possible by biomagnetic means. The past achievements were described in the 8th and 10th International Conferences on Biomagnetism [1,2] and in Andrä et al [3]. In the following sections, a survey of the work performed by some groups in the area will be reviewed and updated, concluding with some possible problems to be tacked by biomagnetic means.

2 Magnetic tracers to study GI motility

2.1 Studies using magnetic markers

Biomagnetic applications to the study of the GI tract started with MM. In 1957 a magnetometer was used to study the motility of the small bowel by having human subjects ingesting a magnetic stirring bar and detecting fluctuations of the magnetic fields produced by changes in its orientation of less than 1 degree relative to the detector [4].

A different marker was used [5], where a magnetized steel sphere (diameter 2 mm) was inserted in a tube, yielding an apparent density D = 1.9 g/cm^3. The MM was ingested and was followed by magnetic measurements made with a SQUID biogradiometer. Sequential mapping combined with MRI allowed the measurement of segmental transit time [6].

In another approach [7] a spherical permanent magnet made with epoxy and microspheres (D=1.4 g/cm^3) was tracked by a fluxgate gradiometer system. The test meal was ingested with MM and other radiopaque markers. Radiographs validated the estimated marker positions and showed that the magnetic marker behaved similarly to the radiopaque markers in the gut. The modeling calculations confirmed adequate precision of the MM localization.

MM has been also useful to study the pharmacodynamics of drug delivery. Insoluble sucrose pellets coated with magnetite and pellets of epoxy mixed with magnetite were prepared. These markers were magnetized in a 0.1 T magnetic field and they were followed using a seven-channel SQUID system [8]. A similar approach was used to study the esophageal, gastric and duodenal transit time [9]. More recently the dissolution of pills was also studied with a 83 channel SQUID system [10]. A 16 channel high Tc SQUID magnetometer placed inside a small shielded enclosure was used to study stomach motility, by recording fields produced by a 1.3 mm diameter steel ball placed at the antrum [11].

2.2 Studies using magnetic tracers

Magnetic tracers can be ingested with a test meal, endowing the GI tract with a strong magnetic signal. Depending on the material used as a tracer either the magnetic permeability or the remanent magnetization can be measured. Thus, changes in magnetic signal would be the correlates of specific processes under study in particular regions of the GI tract.

Frei et al [12] followed by Benmair et al [13] were the first to use a susceptometer driven at 60Hz to study gastric emptying of ferromagnetic tracers of high magnetic permeability. The tracer proved to be innocuous in a previous test as an X-ray contrast agent. The test meal contained a final ferrite concentration of 20 %.

Manganese ferrite powder (3%) mixed with a yogurt was used as a MT to study different functions and parameters of gastrointestinal tract. Firstly, gastric emptying was measured using a portable AC biosusceptometer (ACB) [14]. The instrument can be viewed as two air core transformers, one working as a reference and the other as a measuring transformer. To maximize the signal-to-noise ratio the detection coils are positioned as near the subject as possible, and phase sensitive detection is employed. It can be shown that the signal amplitude is very sensitive to the distance of the magnetic material from the detector ($\sim r^{-6}$) and this was exploited to measure gastric contractions [15].

This same instrument was used to measure the orocaecal transit time [16,17] with advantages over the method of the hydrogen expired breath, produced by a lactulose test meal.

Partial esophagus transit time (ETT) was studied with the same marker and a variation of the test meal [18]. Pharyngeal clearance and transit was also measured using the same approach [19].

In a second category of experiments the test meal was magnetized and the remanent field was measured using a fluxgate magnetometer [20, 21,22]. The decay of magnetization clearly shows the stomach slow waves (SSW) and contains information relevant to the mixing function of the stomach, although some modeling assumptions are necessary to ascertain this relationship. Stomach emptying was also studied through remanent magnetization measurements [23].

The measurements done up to now with MM use a single or a small number of detectors, thus only information about segments of the GI tract that are relatively fixed is obtained. An interesting alternative would be the use of several detectors to produce an image of the distribution of MM over all the viscera, a pilot study was recently published [24].

3 The magnetic detection of electrical activity of the gastrointestinal tract

The detection of magnetic fields produced by the electrical currents occurring in the gastrointestinal tract had to wait until very recently when SQUID detectors were employed. Measurements of gastric signals were initially performed in humans in an unshielded environment [25] and more recently in shielded enclosures in animals and humans [26,27,28,29]. The gastric electrical activity known as Basic Electric Rhythm (BER) was detected with good signal/noise in normal subjects and during tachygastric episodes. It the last case it was shown that there is no migrating electrical activity along the stomach [26]. Spatial temporal characteristics of this signal was also studied with multichannel systems [28].

Measurements of magnetic fields produced by the small intestine, which are quite different from those recorded from the stomach were performed. Electrically, the gastric signals are easier to detect because there is less internal fat near the stomach; however, small bowel signals are virtually impossible to see electrically without extensive adaptive filtering. Magnetically, the small bowel signals are quite clear. In some studies, animals had their gut exposed by surgery and the magnetic signals associated with the small intestine electrical activity was measured. A vector magnetometer was used to detect the magnetic field vector and using this information it was possible to locate the position of the electric sources in the stomach and gut [27]. It was shown that the magnetic measurements could diagnose the intestinal ischemia induced in rabbits by the administration of thrombin or produced by a mechanical occlusion [29]. This experiment simulated the clinically important case of mesenteric vessel thrombosis, which has no method of early detection and is associated with high mortality. It was shown that when the blood supply is reduced in the small intestine, an abnormally electric activity can be recorded [30].

One important point that still needs more efforts in these measurements is an appropriate modeling of the signals [31]. What most groups use is an equivalent current dipole (ECD) that can be thought as a first approximation to the problem of dealing with large areas of electrically excited tissues.

4 Discussion

The future of the biomagnetic methodology in gastroenterology is linked to numerous facts. First, it is necessary to find applications where biomagnetic measurements can provide unique information, or the information provided by existing methods are poor when compared to that obtained by biomagnetic measurements. Second, the instrumentation used should be affordable to hospitals, and if possible of simple operation and low cost. Third, other aspects of the GI tract should be investigated. For instance: basic studies of the esophagus motility, like shortening during swallowing, all the current physiological images done today could be performed in the future employing magnetic tracers instead of radioactive ones. The methods used so far could be classified more as feasibility studies and more exploration should be done on patients with different diseases to show the ability of the biomagnetic approach to diagnosis pathological conditions. Other studies, such as pancreatic and biliary flow measurements should be tried. The connection between the central nervous system and the enteric nervous system offers also many possibilities to explore new frontiers.

It is strongly believed that there is an enormous space for improvements in the examples above mentioned that could lead to new applications and refinements in the present research and diagnose methods in gastroenterology.

Acknowledgements

We are grateful to the partial financial support of the agencies: FAPESP, CNPq, CAPES, TWAS and PRONEX.

References

1. *Biomagnetism: Clinical Aspects*, M.Hoke, S.N. Erné, Y.C. Okada, and G.L. Romani, Amsterdam, Excerpta Medica, 1992.
2. O. Baffa, M. Basile, A. Bradshaw, M. Forsman, Y. Nakaya, and W.O. Richards, "Biomagnetic Research in Gastroenterology" in *Advances in Biomagnetism Research*, C. Aine, Y. Okada, G. Stroink, S. Swithenby and C. Wood, Eds., Springer-Verlag, New York, in press.
3. M. Forsman , "Magnetism in Gastroenterology", in *Magnetism in Medicine,* W. Andrä and H. Nowak, Eds. Berlin: Wiley VCH, 1998, pp. 430-445.
4. M.A. Wenger, E.B. Henderson and J.S. Dinning, "Magnetic method for recording gastric motility", *Science*, 990-991, 1957.
5. S. Di Luzio, S. Comani, G.L. Romani, M. Basile, C. Del Gratta, and V. Pizzela, "A biomagnetic method for studying gastro-intestinal activity", *Il Nuovo Cimento*, **11D(12)**, 1853-1859,1989.
6. M. Basili, M.Neri, A. Carriero, S. Casciardi, S. Comani, C. Del Gratta, L.G. Donato, S. Di Luzio, M.A. Macri, A. Pasquarelli, V. Pizzela, and G.L. Romani, "Measurement of segmental transit time in man" *Digestive Disease Sciences*, **37**, 1537-1543, 1992.
7. M Forsman, L. Hultin and H. Abrahamsson "Measurements of Gastrointestinal Transit Using Fluxgate Magnetometers", in *Biomagnetism: Fundamental Research and Clinical Applications*, L. Decke, C. Baum-gartner, G. Stroink and S.J Williamson, Eds. Amsterdam: Elsevier, 1993, pp 739-742.
8. W. Weitschies, J. Wedemeyer, R. Stehr, and L. Trahms, "Magnetic markers as a noninvasive tool to monitor gastrointestinal transit", *IEEE Trans. on Biomed. Eng.,* **41**, 192-195, 1994.
9. W. Weitschies, D. Cordini, M. Karaus, L. Trahms and W. Semmler, "Magnetic markers monitoring of esophageal, gastric and duodenal transit time of non-disintegrating capsules", *Pharmazie*, **54**, 426-430,1999.
10. L. Trahms, D. Cordini, M. Karaus, J. Breitkreuz and W. Weitschies, "Desintegration of magnetic markers during gastrointestinal transport", *this volume*.
11. M. Nomura, T. Saijyo, Y. Haruta, H. Itozaki, H. Toyoda, Y. Nakaya, S. Ito, and H. Kado, "Biomagnetic measurement of gastric mechanical motility using a high-temperature SQUID imaging", *Advances in Biomagnetism Research,* C. Aine, Y. Okada, G. Stroink, S.

Swithenby, and C. Wood, Eds., Santa Fé, Springer-Verlag, (2000) in press.

12. E.H. Frei, Y. Benmair, Y. Yerashalmi and F. Dreyfuss, "Measurements of the emptying of the stomach with a magnetic tracer", *IEEE Trans. Magn.* **6**, 348-349, 1970.
13. Y. Benmair, F. Dreyfuss, B. Fischel, E.H. Frei, and T. Gilat, "Study of gastric emptying using a ferromagnetic tracer", *Gastroenterology*, **73**, 1041-1045,1977.
14. J.R. Miranda, O. Baffa, R.B. de Oliveira, and N.M. Matsuda, "An AC Biosusceptometer to Study Gastric Emptying", *Med. Phys.* **19**, 445-448, 1992.
15. O. Baffa, R.B. Oliveira, J.R. Arruda Miranda and L.E.A. Troncon, "Analysis and Development of a Simple AC Biosusceptometer for Orocaecal Transit Time Measurements", *Med. & Biol. Eng. & Comput.*, **33**,353-357, 1995.
16. J.R.A. Miranda, R.B. Oliveira, P.L. Sousa, F.J.H. Braga, and O. Baffa**, "**A novel bio-magnetic method to study gastric antral contractions**",** *Phys. Med Biol.* **42**, 1791-1799, 1997.
17. N.A. Daghastanli, F.J.H.N. Braga, R.B. Oliveira and O. Baffa, "Oesophageal Transit Time Evaluated by a Biomagnetic Technique", *Physiol. Meas.***19**, 413-420, 1998.
18. R.B. Oliveira, O. Baffa, L.E.A. Troncon, J.R. A. Miranda and C.R. Cambrea., "Evaluation of a Biomagnetic Technique for Measurement of Orocaecal Transit Time", *Eur. J. Gastroent. & Hepatol.* **8**, 491-496, 1996.
19. C.A. Miquelin, F.J.H.N. Braga, R.O. Dantas, R.B. Oliveira, and O. Baffa., "Pharyngeal Clearance and Pharyngeal Transit Time Determined by a Biomagnetic Method in Normal Humans", *Dysphagia* (2000) in press.
20. O. Baffa, R.B. Oliveira, J.R.A. Miranda, and P.L. Sousa, "Mixing Power of Food in the Stomach Evaluated by a Biomagnetic Technique", *in Biomagnetism: Fundamental Research and Clinical Applications. Studies in Applied Electromagnetics and Mechanics*, C. Baumgartner, L. Deecke, G. Stroink, S.J. Williamson, Eds. Elsevier Sci. Publ. pp 753-756, 1995.
21. A.A.O. Carneiro, O. Baffa and R. B. Oliveira, "Study of Stomach Motility Using Magnetic Tracers", *Phys. Med Biol.* **44**,1691-1697, 1999.
22. M. Forsman, "Intragastric movement assessment by measuring magnetic field decay of magnetised tracer particles in a solid meal, *Med Biol Eng Comput* **38**, 169-174, 2000.
23. M. Forsman, "Gastric emptying of solids measured by means of magnetised iron oxide powder", *Med Biol Eng Comput* **36**, 2-6, 1998.
24. M. Moreira, L.O. Murta Jr. and O. Baffa. "Imaging Ferromagnetic Tracers With an AC Biosusceptometer", *Rev. Sci. Instrum.* **71**, 2532-2538, 2000.
25. S. Comani, M. Basile, S. Casciardi, C. Del Gratta, S. Di Luzio, S.N. Erné, M. Macri, M. Neri, M. Peresson, and G.L. Romani, "Extracorporeal direct magnetic measurement of gastric activity", in *Biomagnetism: Clinical Aspects*, M. Hoke, S.N. Erné, Y. Okadaand G.L. Romani, Eds. Amsterdam Excerpta Medica, 1992, pp.639-642.
26. H.D. Allescher, K. Abraham-Fuchs, R.E. Dunkel and M. Classen, "Biomagnetic 3-dimensional spatial and temporal characterization of electrical activity of human stomach", *Dig, Dis. Sci.***43**, 683-693, 1998.
27. L. Alan Bradshaw, J.K. Ladipo, D.J. Stanton and., "The human vector magnetogastrogram", *IEEE Trans. Biomed. Eng.***46**, 959-970, 1999.
28. G.K. Turnbull, S.P. Ritcey, G. Stroink, B. Brandts and P. van Leeuwen, "Spatial and temporal variations in the magnetic fields produced by human gastrointestinal activity", *Med Biol Eng Comput* **37**, 549-554, 1999.
29. S.A. Siedel, S.S. Hedge, L. Alan Bradshaw, J.K. Ladipo, J.P. Wiswo Jr and W.O. Richards, "Non invasive detection of ischemic bowel", *J.Vasc.Surg.* **30**, 309-319, 1999.
30. S.A. Siedel, S.S. Hedge, L. Alan Bradshaw, J.K. Ladipo and W.O. Richards, "Intestinal tachyarrythmias during small bowel ischemia", *Am. J. Physiol.,.***277,** G993-G999, 1999.
31. E.R. Moraes and O. Baffa, "Modelling of Magnetogastrography Signal", in *Recent Advances in Biomagnetism*, T. Yoshimoto, M. Kotani, S. Kuriki, H. Karibe, and N. Nakasato, Eds. Sendai: Tohoku University Press, 1999, pp. 262-265.